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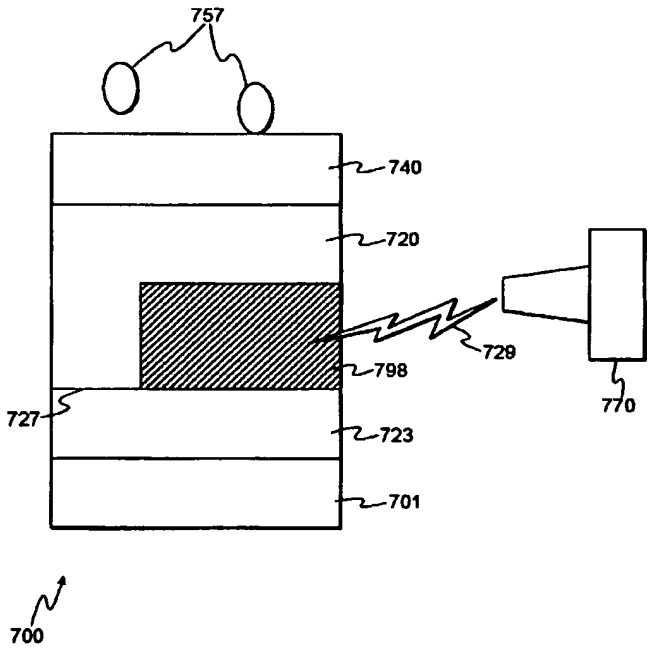

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(57) Abstract: A sensor (700) for detecting analytes of interest in which natural or synthetic macromolecules (740) are immobilized on an electrically conductive base member (720) to insure that interaction of analyte with the macromolecules will lead to altered de novo electrical signals in a sensor circuit (720,770,198).

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AN ANALYTE DETECTION SYSTEM

Background of the Invention.

1. Field of the Invention.

This invention pertains to a sensor and method for detecting or quantifying analytes. More particularly the present invention is directed to the detection of analytes by certain de novo electrical interactions thereof with an immobilized macromolecular binding agent and the analysis of effects that are produced as a result of such interactions.

2. Description of the Related Art.

Chemical and biological sensors are devices that can detect or quantify analytes by virtue of interactions between targeted analytes and macromolecular binding agents such as enzymes, receptors, DNA strands, heavy metal chelators, or antibodies. Such sensors have practical applications in many areas of human endeavor. For example, biological and chemical sensors have potential utility in fields as diverse as blood glucose monitoring for diabetics, detection of pathogens commonly associated with spoiled or contaminated food, genetic screening, and environmental testing.

Chemical and biological sensors are commonly categorized according to two features, namely, the type of material utilized as binding agent and the means for detecting an interaction between binding agent and targeted analyte or analytes. Major classes of biosensors include enzyme (or catalytic) biosensors, immunosensors and DNA biosensors. Chemical sensors make use of synthetic macromolecules for detection of target analytes. Some common methods of detection are based on electron transfer, generation of chromophores, or fluorophores, changes in optical or acoustical properties, or alterations in electric properties when an electrical signal is applied to the sensing system.

Enzyme (or catalytic) biosensors utilize one or more enzyme types as the macromolecular binding agents and take advantage of the complementary shape of the selected enzyme and the targeted analyte. Enzymes are proteins that perform most of the catalytic work in biological systems and are known for highly specific catalysis. The shape and

reactivity of a given enzyme limit its catalytic activity to a very small number of possible substrates. Enzymes are also known for speed, working at rates as high as 10,000 conversions per second per enzyme molecule. Enzyme biosensors rely on the specific chemical changes related to the enzyme/analyte interaction as the means for determining the presence of the targeted analyte. For example, upon interaction with an analyte, an enzyme may generate electrons, a colored chromophore or a change in pH (due to release of protons) as the result of the relevant catalytic enzymatic reaction. Alternatively, upon interaction with an analyte, an enzyme may cause a change in a fluorescent or chemiluminescent signal that can be recorded by an appropriate detection system.

Immunosensors utilize antibodies as binding agents. Antibodies are protein molecules that bind with specific foreign entities, called antigens, which can be associated with disease states. Antibodies attach to antigens and either remove the antigens from a host and/or trigger an immune response. Antibodies are quite specific in their interactions and, unlike enzymes, they are capable of recognizing and selectively binding to very large bodies such as single cells. Thus, antibody-based biosensors allow for the identification of certain pathogens such as dangerous bacterial strains. As antibodies generally do not perform catalytic reactions, there is a need for special methods to record the moment of interaction between target analyte and recognition agent antibody. Changes in mass (surface plasmon resonance, acoustic sensing) are often recorded; other systems rely on fluorescent probes that give signals responsive to interaction between antibody and antigen. Alternatively, an enzyme bound to an antibody can be used to deliver the signal through the generation of color or electrons; the enzyme-linked immunosorbent assay (ELISA) is based on such a methodology.

DNA biosensors utilize the complementary nature of the nucleic acid double-strands and are designed for the detection of DNA or RNA sequences usually associated with certain bacteria, viruses or given medical conditions. A sensor generally uses single-strands from a DNA double helix as the binding agent. The nucleic acid material in a given test sample is then denatured and exposed to the binding agent. If the strands in the test sample are complementary to the strands used as binding agent, the two interact. The interaction can be monitored by various means such as a change in mass at the sensor sur-

face or the presence of a fluorescent or radioactive signal. Alternative arrangements provide binding of the sample of interest to the sensor and subsequent treatment with labeled nucleic acid probes to allow for identification of the sequences of interest.

Chemical sensors make use of non-biological macromolecules as binding agents. The binding agents show specificity to targeted analytes by virtue of the appropriate chemical functionalities in the macromolecules themselves. Typical applications include gas monitoring or heavy metal detection; the binding of analyte may change the conductivity of the sensor surface or lead to changes in charge that can be recorded by an appropriate field-effect transistor (FET). Several synthetic macromolecules have been used successfully for the selective chelation of heavy metals such as lead.

The present invention has applicability to all of the above noted binding agent classes.

Known methods of detecting interaction of analyte and binding agent can be grouped into several general categories: chemical, optical, acoustical, and electrical. In the last, a voltage or current is applied to the sensor surface or an associated medium. As binding events occur on the sensor surface, there are changes in electrical properties of the system. The leaving signal is altered as function of analyte presence.

The most relevant prior art to the present invention involves sensors that are based on electrical means for analyte detection. There are several classes of sensors that make use of applied electrical signals for determination of analyte presence. Amperometric sensors make use of oxidation-reduction chemistries in which electrons or electrochemically active species are generated or transferred due to analyte presence. An enzyme that interacts with an analyte may produce electrons that are delivered to an appropriate electrode; alternatively, an amperometric sensor may employ two or more enzyme species, one interacting with analyte, while the other generates electrons as a function of the action of the first enzyme, an arrangement known as a coupled enzyme system. Glucose oxidase has been used frequently in amperometric biosensors for glucose quantification for diabetics. Other amperometric sensors make use of electrochemically active species whose presence alters the system applied voltage as recorded at a given sensor electrode. Not all sensing systems can be adapted for electron generation or transfer, and thus many

sensing needs cannot be met by amperometric methods alone. The general amperometric method makes use of an applied voltage and effects of electrochemically active species on said voltage. An example of an amperometric sensor is described in U.S. Patent No. 5,593,852 to Heller, *et al.*, which discloses a glucose sensor that relies on electron transfer effected by a redox enzyme and electrochemically-active enzyme cofactor species.

An additional class of electrical sensing systems includes those sensors that make use primarily of changes in an electrical response of the sensor as a function of analyte presence. Some systems pass an electric current through a given medium; if analyte is present, there is a corresponding change in an exit electrical signal, and this change implies that analyte is present. In some cases, the binding agent-analyte complex causes an altered signal, while in other systems, the bound analyte itself is the source of changed electrical response. Such sensors are distinguished from amperometric devices in that they do not necessarily require the transfer of electrons to an active electrode. Sensors based on the application of an electrical signal are not universal, in that they depend on alteration of voltage or current as a function of analyte presence; not all sensing systems can meet such a requirement. An example of this class of sensors is U.S. Patent No. 5,698,089 to Lewis, *et al.*, which discloses a chemical sensor in which analyte detection is determined by a change of an applied electrical signal. Binding of analyte to chemical moieties arranged in an array alters the conductivity of the array points; unique analytes can be determined by the overall changes in conductivity of all of the array points. The present invention does not rely on arrays or changes of applied electrical signal as a function of analyte presence. The present sensor does not require any applied electrical or electromagnetic signal.

Several other publications that do not fall into the preceding categories are worthy of mention in the prior art. The document, *Direct Observation of Enzyme Activity with the Atomic Force Microscope*. Radmacher, Manfred *et al.* Science 265:1577, 9 September 1994 noted the existence of augmented spatial fluctuations in enzymes interacting with substrates, but did not apply this phenomenon to analyte detection.

U.S. Patent No. 5,620,854 to Holzrichter, *et al.*, proposed the use of macromolecule motion to detect analyte. The disclosed system relies specifically on atomic force or scanning tunneling microscopes for detection of said motion.

U.S. Patent No. 5,114,674 to Stanbro, *et al.* discloses a sensor that is based on the interference of applied electrical fields. Interaction of target analyte with a binding agent alters the interference of the applied electrical field.

Other prior-art voltage-based sensors require the use of semiconducting field-effect transistors and rely on the chemical generation or physical trapping of charged species near the sensor surface. This approach has found widespread use in the detection of positively-charged heavy metals as well as analytes that are involved in proton (H+) generating enzyme reactions. The document *Endoscopic Urease Sensor System for Detecting Helicobacter pylori on Gastric Mucosa*, Sato *et al.* Gastrointestinal Endoscopy 49: 32-38 (1999) describes a pH-sensitive FET for the detection of the enzyme urease, associated with the pathogenic bacterium H. pylori.

While hundreds of sensors have been described in patents and in the scientific literature, actual commercial use of such sensors remains limited. In particular, virtually all sensor designs set forth in the prior art contain one or more inherent weaknesses. Some lack the sensitivity and/or speed of detection necessary to accomplish certain tasks. Other sensors lack long-term stability. Still others cannot be sufficiently miniaturized to be commercially viable or are prohibitively expensive to produce. Some sensors must be pre-treated with salts and/or enzyme cofactors, a practice that is inefficient and bothersome. To date, virtually all sensors are limited by the known methods of determining that contact has occurred between an immobilized binding agent and targeted analytes. Use of fluorescent or other external detection probes adds to sensor production requirements and reduces lifetimes of such sensor systems. Additionally, the inventor believes that there is no sensor method disclosed in the prior art that is generally applicable to the vast majority of macromolecular binding agents, including enzymes, antibodies, antigens, nucleic acids, receptors, and synthetic binding agents.

Summary of the Invention.

It is therefore a primary object of some aspects of the present invention to provide an improved analyte detection system, in which a detection unit is electrically connected to a sensor strip so as to allow for detection of de novo electrical currents in a sensor circuit that are responsive to analyte presence.

It is a further object of some aspects of the invention to describe an electrical circuit that includes a sensor strip and a semiconductive element for sensitive, and inexpensive analyte detection.

It is an additional object of some aspects of the invention to improve the consistency and ease of use in detection of an analyte in a sensor system by inclusion of an additional conductive element in the detection circuit.

In contrast to the above noted U.S. Patent No. 5,593,852, the practice of the present invention does not require application of an external voltage, oxidation-reduction chemistry, or electron generation or transfer. Furthermore, in contrast to the above noted disclosures, the present invention does not rely on arrays or changes of applied electrical fields or signals as a function of analyte presence.

The invention is an extension of the sensor and method described in PCT application PCT/US00/15400 of common assignee herewith, and herein incorporated by reference. The sensor disclosed in PCT application PCT/US00/15400 is based on detection of de novo electrical signals, and is capable of rapid determination of analyte presence in complex sample matrices. Structural changes involving contact between electrodes, the sensor strip and the sensor circuit components disclosed herein provide for further improved analyte detection through detection and monitoring of phenomena, including electrical signals, that are generated in a sensor circuit during analyte interaction.

As described in the noted PCT application PCT/US00/15400, which discloses a sensor circuit incorporating a base member, or first conducting element and a binding agent layer associated with the first conducting element. As disclosed in the noted PCT application, the methodology of analyte detection is very sensitive. Using the improvements of the present invention, it is possible to detect specific pathogenic bacteria consistently in a complex meat matrix within two minutes at 1-10 cells per milliliter of sample.

In general, measurement of de novo current in a sensor circuit according to the present invention allows for rapid, specific and sensitive determination of analyte presence.

A sensor strip according to the invention may contain a plurality of identical or unique sensor strips so as to increase system detection redundancy and/or multiple analyte detection capabilities. Component strips of a composite sensor strip may be individually monitored, each component strip forming a part of a different sensor circuit.

In preferred embodiments of the invention sensor strips are unpowered, that is, no electrical signal is applied to them. In other preferred embodiments, the sensor strip may be powered through application of voltage, current, or other electrical signal to the sensor strip. In some embodiments, a plurality of sensor strips may be employed in the detection of one or a plurality of analytes.

Contact with the sensor strip is generally electrically passive in nature and occurs at one or two positions. One of the electrodes may serve as an electron sink or electrical ground. The electrodes may be prepared from either conducting or semiconducting materials or a combination thereof. Components of at least one electrode may be selected from materials that allow for facile hole donation to a semiconductive element. A second conductive element, preferably composed of indium tin oxide, gold or other high work function materials is electrically contacted to the semiconductive element. The electrodes are generally equipotential. In preferred embodiments employing electrically passive electrode contact with the sensor strip, neither electrode is used to deliver an external electrical signal to the unpowered sensor strip. The two electrodes associated with each sensor strip may be prepared from the same or different materials. Electrodes may be completely unnecessary in embodiments that directly generate electroluminescence.

A detection unit is generally contacted to a sensor strip at two positions through passive contact of associated equipotential electrodes and the detection unit generally measures de novo current flow or voltage in a closed circuit. The detection unit may simultaneously measure more than one type of signal and it may be contacted to a plurality of sensor strips. Current measurement may be direct or over a resistor for a voltage reading. A reading or other indication is recorded when a generated current is passed over a voltmeter resistor to yield a value read as a voltage, though the original signal is a de

novo current responsive to analyte presence. Additionally, the detection unit may further process the signal or a component thereof for the purpose of analyte detection and concentration range determination. In some preferred embodiments, a detection unit is unnecessary, as the generated current leads directly or otherwise to electroluminescence.

The invention provides a sensor for detecting an analyte, which includes a base member or first conductive element, a binding agent layer proximate the base member, a semiconductive element proximate the base member, and, a second conductive element that is electrically contacted to the semiconductive element and the base member. The base member and the binding agent layer minimally define a sensor strip, while additional layers such as the semiconductive element or the second conductive element may be included in the term "sensor strip" if they are physically associated with the base member.

An aspect of the sensor includes a chemical entity bound to the base member and disposed proximate the binding agent layer.

Yet another aspect of the sensor includes two equipotential leads coupling the sensor strip to a detection unit, wherein at least one of the equipotential leads is electrically contacted to the semiconductive element.

According to still another aspect of the sensor, the work function of the semiconductive element is intermediate the work functions of the base member and the second conductive element.

According to an additional aspect of the sensor, the second conductive element is an element of an electrode of the detection unit. The second conductive element is brought into contact with the semiconductive element.

One aspect of the sensor includes a packaging layer disposed above the binding agent layer. The packaging layer is soluble in a medium that contains the analyte.

According to another aspect of the sensor, the semiconductive element is an organic compound and is physically associated with the base member on a first side of the base member, and the binding agent layer is immobilized on a second side of the base member.

According to a further aspect of the sensor, the sensor strip includes a plurality of sensor strips.

According to another aspect of the sensor, the semiconductive element is electroluminescent.

The invention provides a method for detecting a predetermined analyte, including the steps of providing an electrically conductive base member, and forming a binding agent layer of macromolecules in proximity to the base member, wherein the macromolecules are capable of interacting at a level of specificity with the predetermined analyte. The method further includes disposing a semiconductive element on the base member, wherein the base member, the binding agent layer and the semiconductive element define a sensor strip, disposing a conductive element proximate the semiconductive element, exposing the predetermined analyte to the binding agent layer, and, detecting an electrical current generated in a closed electrical circuit. The current is responsive to presence of the predetermined analyte. The closed electrical circuit minimally includes the base member, the semiconductive element, and a second conductive element electrically contacted to the semiconductive element and the base member.

An aspect of the method includes binding a chemical entity to the base member, and forming the binding agent layer proximate the chemical entity.

In another aspect of the method, detecting is performed by equipotentially coupling leads of a detection unit to the sensor strip, wherein one of the leads is coupled to the semiconductive element.

In a further aspect of the method, coupling the detection unit is performed by contacting electrical leads to the sensor strip and the semiconductive element. Electrical passivity of the leads is maintained during coupling.

In yet another aspect of the method, the conductive element is physically associated with one of the leads prior to coupling.

According to still another aspect of the method, the work function of the conductive element is less than the work function of the semiconductive element and the work function of the conductive element is greater than the work function of the base member.

According to an additional aspect of the method, the semiconductive element is an organic compound, and is physically associated with the base member on a first side of the base member. The binding agent layer is immobilized on a second side of the base member.

One aspect of the method includes disposing a packaging layer above the binding agent layer. The packaging layer is soluble in a medium that contains the predetermined analyte.

Still another aspect of the method includes generating photonic energy in the closed electrical circuit, the photonic energy being detected remote from the sensor strip.

According to another aspect of the method, the sensor strip includes a plurality of sensor strips.

The invention provides a sensor for the detection of an analyte through generated electroluminescence, including a base member that has a conductive property, a binding agent layer proximate the base member, a electroluminescent semiconductive element proximate the base member, and a second conductive element that is electrically contacted to the base member and the semiconductive element.

According to an aspect of the sensor, the work function of the semiconductive element is intermediate the work functions of the base member and the second conductive element.

According to yet another aspect of the sensor, the second conductive element is optically opaque.

Brief Description of the Drawings.

For a better understanding of these and other objectives of the present invention, reference is made to the following detailed description of the invention, by way of example, which is to be read in conjunction with the following drawings, wherein:

Fig. 1 is a schematic view of a sensor detection system (100), which is constructed and operative in accordance with a preferred embodiment of the invention, wherein a sensor strip (122) comprised of base member (120), chemical entity (132), binding agent

layer (140) and packaging layer (150) forms a closed sensor circuit with electrodes (160, 161), semiconductive element (198) and detection unit (170);

Fig. 2 is a plot (200) of data from a control experiment, using the system shown in Fig. 1, in which the binding agent was a monoclonal antibody for pathogen, *E. coli* 0157:H7;

Fig. 3 is a plot (300) of data from an the experiment performed under the conditions of the experiment shown in Fig. 2, in which target analyte was present;

Fig. 4 is a schematic view of a sensor detection system (400), which is constructed and operative in accordance with an alternative embodiment of the invention, wherein a semiconductive element (498) is associated with a sensor strip (422);

Fig. 5 is a schematic view of a sensor detection system (500), which is constructed and operative in accordance with an alternative embodiment of the invention, wherein a semiconductive element (598) is placed between base member (520) having a low work-function, and a second conductive element (597) having a high work function;

Fig. 6 is a schematic view of a multiplexed alternative embodiment of a sensor detection system (600), which is constructed and operative in accordance with an alternate embodiment of the invention;

Fig. 7 is a schematic view of a sensor detection system (700), which is constructed and operative in accordance with an alternate embodiment of the invention, wherein analyte-responsive generated current is detected through electroluminescence produced by the sensor system; and

Fig. 8 is a schematic view of sensor system (800), which is constructed and operative in accordance with an alternate embodiment of the invention showing a sensor strip (822) in contact with sample (853).

Description of the Preferred Embodiment.

In the following description, numerous specific details are set forth in order to provide a thorough understanding of the present invention. It will be apparent, however, to one skilled in the art that the present invention may be practiced without these specific

details. In other instances well-known circuits and control logic have not been shown in detail in order not to unnecessarily obscure the present invention.

Definitions.

Certain terms are now defined in order to facilitate better understanding of the present invention.

An "analyte" is a material that is the subject of detection or quantification.

"Work function" is the electronic work function, which is the energy required to move an electron from the Fermi level to the vacuum level.

A "base member" is a solid or liquid element on or near which macromolecules can be physically or chemically immobilized for the purpose of analyte detection.

"Macromolecules", "macromolecular binding agents", "binding agents" or "macromolecular entities" can be any natural, mutated, synthetic, or semi-synthetic molecules that are capable of interacting with a predetermined analyte or group of analytes at a level of specificity.

A "binding agent layer" is a layer proximate the base member and composed of one or a plurality of binding agents. The binding agent layer may be composed of more than one type of binding agent. A binding agent layer may additionally include molecules other than binding agents. Cross-linking agents may be applied to bind separate components of a binding agent layer together.

A "chemical entity" is a chemical layer that is disposed proximate the base member on either one or both sides of the base member. It may serve to partially insulate the base member from direct contact with binding agents, or it may serve as the semiconductive element defined below. Chemical entities may be differentially deposited on opposite sides of a base member by any means or multiple layers on a given side of the base member may be considered a single chemical entity. Natural oxides may serve the role of chemical entity.

A "packaging layer" is defined as a chemical layer disposed above the binding agent layer. The packaging layer may aid in long term stability of the macromolecules, and in the presence of a sample that may contain analyte of interest, the packaging layer

may dissolve to allow for rapid interaction of analyte and binding agents. The packaging layer may also serve in conjunction with the charged macromolecules in the role of a semiconductive element defined below. Such may be the case when a sensor is coated equally on both sides with chemical entities, macromolecules, and packaging layer.

A "sensor strip" is defined as a minimum of a single base member and its associated binding agent layer. If multiple macromolecular entities, chemical entities, packaging layers or other elements are physically associated with the base member, then they are included in the term "sensor strip".

An "electrode" or "lead" is a wire, electrical lead, connection, electrical contact or the like that is attached at one end to a detection unit and contacted at the other end directly or indirectly to a sensor strip.

The terms "generated" and "de novo" electrical signals are used with respect to the electrical arts. Specifically by these terms, it is intended to exclude obligate oxidation-reduction chemistries and electrical phenomena resulting directly or otherwise from the necessary application of an external electrical or electromagnetic signal to sensor strip or sample. A generated or de novo electrical signal in the present invention is one that is produced in a sensor circuit as described herewith without any required application to the sensor strip of electrical or electromagnetic signal. Additionally, there is no oxidative transfer of electrons between the base member and binding agent, analyte, or sample.

A "detection unit" is any device or material that allows for the detection of one or more electrical signals generated in a sensor circuit.

"Semiconductive element" refers to a material of semiconductive property included in a "sensor circuit" that minimally includes one such element in addition to a base member or first conductive element, and a second conductive element. The semiconductive element may be present as a coating, chip or other form.

A "second conductive element" is an electrically-conducting material that is electrically contacted to the semiconductive element and is distinct from the conductive base member. The second conductive element is electrically contacted to the base member, either directly or through the components of a sensor circuit. Coatings of high work function metals such as gold and indium-tin oxide are preferred in the role of second conduc-

tive element when the base member is a low work function metal. Alternatively, if the base member is a high work function metal, the second conductive element may be a low work function metal such as calcium or aluminum.

Without being bound by any particular theory, the following discussion is offered to facilitate understanding of the invention. The sensor design disclosed herein is based on de novo electrical signals generated in a sensor circuit as a function of analyte presence. The sensor utilizes a novel method of detecting an analyte wherein macromolecular binding agents are first immobilized as a binding agent layer proximate an electrically conductive base member. De novo electrical signals such as current in a circuit that includes the base member can be monitored for change during exposure of the macromolecular binding agents to a sample that may contain target analyte. In the present invention, the advantages of particular forms of sensor strip contact are disclosed more fully. Specifically, a semiconductive element placed between base member and a second conductive element may be utilized in order to facilitate signal measurement and analyte detection. The semiconductive element may be electroluminescent.

In the various embodiments disclosed herein, like elements have like reference numerals differing by multiples of 100.

First Embodiment.

Reference is now made to Fig. 1, which is a schematic of a sensor detection system (100) that is constructed and operative in accordance with a preferred embodiment of the invention. The sensor detection system (100) comprises a sensor strip (122), which is part of a sensor circuit (120, 160, 170, 161, 197, 198) in which one or more electrical signals are generated internally in the sensor circuit (120, 160, 170, 161, 197, 198) itself. Provision is made for an external detection unit (170) to be coupled to the sensor strip (122) using equipotential, electrically-passive electrodes (160, 161) to provide contact between the sensor strip (122) and the detection unit (170). The equipotential passive electrodes (160, 161) of the detection unit (170) are contacted to the sensor strip (122) at a contact position (165) and to a semiconductive element (198) at a contact position (167). The electrode (161) is provided with a second conductive element (197) in the

form of a gold coating. In Fig. 1, the electrode (161) and the second conductive element (197) are shown in a non-contacting relationship with the sensor strip (122) for clarity of presentation, it being understood that in operation the second conductive element (197) is contacted with the semiconductive element (198), as indicated by the double-headed arrow.

The sensor circuit (120, 160, 170, 161, 197, 198) superficially models metal-semiconductor-metal organic light-emitting diodes (OLED's) with metal-insulator-metal (MIM) or metal-semiconductor-metal (MSM) structure. The purpose of the semiconductive element (198) is to aid in facile signal capture. The semiconductive element (198) may be present as a coating, chip or other form. The presence of at least one semiconductive element (198) between a base member (120) and the second conductive element (197) facilitates measurement of de novo electrical signals in the sensor circuit (120, 160, 170, 161, 197, 198). Interaction of analyte (155, 157) with a binding agent layer (140) causes perturbation of the electron cloud in the base member (120). Analyte-associated electrostatic fields drive electrons from the base member (120) into the semiconductive element (198), with concomitant motion of holes from the second conductive element (197) into the semiconductive element (198). The holes and electrons recombine in the semiconductive element (198). In some embodiments, light is generated, as is explained hereinbelow with reference to Fig. 7. In other embodiments holes flow through the detection unit (170) and allow for current measurement. Hole motion through the detection unit (170) is an analyte-responsive signal.

In general, metals having low work functions are preferred for the base member (120).Conducting and semiconducting foils, coatings, thin-films, inks, and solid pieces are particularly preferred for the base member (120).

The semiconductive element (198) is preferably prepared from organic compounds and has a work function between those of the base member (120) and the second conductive element (197). Examples of appropriate semiconductive elements include, but are not limited to semiconductive coatings, organic polymers, and the like. Semiconductive elements may be incorporated directly into detection unit, associated electrodes or sensor

strips, although in Fig. 1, the semiconductive element (198) is shown as a distinct structure for clarity of presentation.

Semiconductive elements may be incorporated directly into detection unit, associated electrodes or sensor strips and are shown as a distinct elements in the accompanying figures for the purpose of convenience of presentation.

In particular applications, work functions for the base member (120), the semiconductive element (198), and the second conductive element (197) are selected for optimal delivery of base member electrons and electrode holes into the semiconductive element (198). It is believed that electrons and holes combine in the semiconductive element (198) to form excitons.

The detection unit (170) may then measure a current, or other electrical signal generated in the sensor circuit (120, 160, 170, 161, 197, 198) as a function of analyte interaction with the sensor strip, as is disclosed in further detail hereinbelow.

The detection unit (170) may also serve to ground the sensor strip (122) prior to measurement, so that stray signals are removed prior to exposure of sample to the sensor strip (122). Such grounding may be performed either through an optional switched grounding electrode (168) or using a separate contact between the detection unit (170) and the sensor strip (122) (not shown). Grounding may also be performed at times during operation of the sensor detection system (100) in order to enhance signal quality.

The binding agent layer (140) is located proximate the base member (120). A chemical entity (132) is disposed between the base member (120) and the binding agent layer (140). Self-assembled monolayers are particularly preferred in the role of the chemical entity (132). Typically, the chemical entity (132) is a self-assembled monolayer ("SAM") formed proximate the base member, with binding agent layer (140) disposed above the SAM. For the purposes of this invention, "proximate" with respect to the binding agent layer (140) disposition relative the base member is defined as any distance that allows for analyte-responsive generation of a de novo electrical signal in the sensor circuit (120, 160, 170, 161, 197, 198) as defined hereinabove.

An optional packaging layer (150), shown on the left side of Fig. 1, is a layer of water-soluble chemicals deposited above the immobilized macromolecules of the binding

agent layer (140). The packaging layer (150) may be deposited by soaking or spraying methods. The packaging layer (150) serves to stabilize the binding agent layer (140) during prolonged storage. In the absence of a packaging layer, oil and dirt may build up on the hydrophilic binding agent layer (140) and may interfere with the rapid action of the sensor system. Glucose and a salt, such as sodium chloride, are typically used for the packaging layer (150) so as to guarantee their dissolution in aqueous samples, and thus facilitate direct interaction between macromolecular binding agents of binding agent layer (140) and analytes (157). Other chemicals may be chosen for use in the packaging layer. Water-soluble polymers, sugars, salts, organic, and inorganic compounds are all appropriate for use in preparation of the packaging layer (150).

As shown on the left side of Fig. 1, free analyte (155) is disposed proximate the packaging layer (150) prior to its dissolution. When the packaging layer (150) dissolves, the macromolecules incorporated in the binding agent layer (140) are free to immediately interact with analyte (157), as shown on the right side of Fig. 1. After dissolution of the packaging layer (150), analyte (157) is shown interacting with the binding agent layer (140) on the right side of Fig. 1. The analyte (155, 157) can be a member of any of the following categories, listed herein without limitation: cells, organic compounds, antibodies, antigens, virus particles, pathogenic bacteria, metals, metal complexes, ions, spores, yeasts, molds, cellular metabolites, enzyme inhibitors, receptor ligands, nerve agents, peptides, proteins, fatty acids, steroids, hormones, narcotic agents, synthetic molecules, medications, enzymes, nucleic acid single-stranded or double-stranded polymers. The analyte (155) can be present in a solid, liquid, gas or aerosol. The analyte (155) could even be a group of different analytes, that is, a collection of distinct molecules, macromolecules, ions, organic compounds, viruses, spores, cells or the like that are the subject of detection or quantification. Some of the analyte (157) physically interacts with the sensor strip (122) after dissolution of the packaging layer (150) and causes an increase in electrical signals generated in the sensor circuit (120, 160, 170, 161, 197, 198). Contact of electrodes (160, 161) to sensor strip (122) and semiconductive element (198) allows for measurement of such a de novo electrical signal that is responsive to analyte presence. There is no requirement for application of a voltage or other electrical signal to

the sensor strip (122) prior to or during measurement of generated electrical signals by the detection unit (170). In some embodiments, one may apply such an external signal, in which case the generated electrical signal in the sensor system that is responsive to analyte presence will alter the exit signal.

Examples of macromolecular binding agents suitable for use as the binding agent layer (140) include, but are not limited to enzymes that recognize substrates and inhibitors, antibodies that bind antigens, antigens that recognize target antibodies, receptors that bind ligands, ligands that bind receptors, nucleic acid single-strand polymers that can bind to form DNA-DNA, RNA-RNA, or DNA-RNA double strands, and synthetic molecules that interact with targeted analytes. The present invention can thus make use of enzymes, peptides, proteins, antibodies, antigens, catalytic antibodies, fatty acids, receptors, receptor ligands, nucleic acid strands, as well as synthetic macromolecules in the role of the binding agent layer (140). Natural, synthetic, semi-synthetic, over-expressed and genetically-altered macromolecules may be employed as binding agents. The binding agent layer (140) may form monolayers, multilayers or mixed layers of several distinct binding agents or binding agents with other chemical components (not shown). A monolayer of mixed binding agents may also be employed (not shown). The binding agents in the binding agent layer (140) may be cross-linked together with glutaraldehyde or other chemical cross-linking agents.

The macromolecule component of the binding agent layer (140) is neither limited in type nor number. Enzymes, peptides, receptors, receptor ligands, antibodies, catalytic antibodies, antigens, cells, fatty acids, synthetic molecules, and nucleic acids are possible macromolecular binding agents in the present invention. The sensor detection system (100) may be applied to detection of many classes of analyte because it relies on the following properties shared by substantially all applications and embodiments of the sensor detection system according to the present invention:

(1) that the macromolecules chosen as binding agents are highly specific entities designed to bind only with a selected analyte or group of analytes;

(2) that analytes have associated electrostatic fields;

(3) that binding of analyte electrostatically induces electrons from the conducting base member into the semiconductive element; and

(4) that the resulting positive charge in the base member and second conductive element leads to hole delivery to the semiconductive element and analyte-associated current.

The broad and generally applicable function of the sensor detection system (100) is preserved during formation of the binding agent layer (140) in proximity to the base member (120) because the binding agent layer (140) formation can be effected by either specific covalent attachment or general physical absorption. It is to be emphasized that the change in de novo signal that is associated with analyte presence does not depend on any specific enzyme chemistries, optical effects, fluorescence, chemiluminescence, oxidation-reduction phenomena or applied electrical signals. Additionally, there are no reference electrodes, and the two detection unit electrodes are generally equipotential prior to measurement of signal generated in the sensor circuit. These features are important advantages of the present invention. Additionally, during operation of the sensor detection system (100), current is actually generated, and the generated electricity may be of use in color-based analyte detection systems that do not require use of a detection unit. Excitons produced by hole-electron combination in the semiconductive element (198) can produce light visible to the human. The semiconductive element (198) may be an organic light emitting material.

The detection unit (170) is any device or material that can detect one or more de novo signals in a sensor circuit as a result of sensor strip exposure to a sample that contains analyte (155). Examples of such signals include but are not limited to electrical current; magnetic field strength; induced electromotive force; voltage; light; impedance; signal sign; frequency component or noise signature of a predetermined electrical signal propagated into a sensor strip at a first location and received at a second location. While the detection unit (170) may be a digital electrical metering device, it may also have additional functions that include, but are not limited to sensor strip grounding, data storage, data transfer, data processing, alert signaling, command/control functions, and process control. Detection units may be contacted through "leads", realized as electrodes to one

or a plurality of sensor strips. The detection unit (170) may be a digital voltmeter. In any case, the de novo signal produces a reading or indication in the detection unit (170). In some embodiments, the de novo signal may be an electrical voltage or a current, and the reading or indication can be a voltage value measured over an internal resistor of the detection unit (170).

Baseline readings in the detection unit (170) may be determined from a sample that lacks target analyte or analytes or by grounding the sensor strip (122) prior to sample exposure in a manner disclosed above.

The specific design of the detection unit (170) depends on what quantity or quantities are being observed, e.g., current, magnetic field flux, frequency, impedance. The detection unit may be integrated into a computer (not shown) or other solid-state electronic device for easier signal processing and data storage. The same or a different computer may be used to control sample application or sample serial dilution in order to monitor both sample manipulation as well as the generated electrical responses in a single or multiplexed sensor strip arrangement. The detection unit may also be a voltage-sensitive dye or colored material.

The implications of the analyte detection methodology are significant. Firstly, detection can take away from the direct point of macromolecule-analyte contact, as the electrons and holes can recombine in the semiconductive element at a point removed from analyte-macromolecule interaction. This fact allows for closed-package "food sensing" or the sensing of potentially hazardous samples, e.g. blood in closed containers. One portion of the sensor contacts the material of interest, while detection of analyte-responsive de novo electrical signals occurs between on the exposed portion of the sensor strip.

The implications are that nearly any material that can be recognized at a level of specificity by a peptide, protein, antibody, enzyme, receptor, nucleic acid single strand, synthetic binding agent, or the like can be detected and quantified safely in food, body fluids, air or other samples quickly, cheaply, and with high sensitivity. Response is very rapid, generally less than 90 seconds. Cost of manufacture is low, and sensitivity has been shown to be very high.

Example 1.

The analysis in this example was performed using the embodiment of Fig. 1. Ground turkey meat (5.11 g) was re-suspended in deionized water (40 ml). The suspension was vortexed and used as a background for detecting a specific bacterial strain. Sensor strips specific for pathogen *E. coli* 0157:H7 were prepared as follows. Aluminum foil having a matte surface and a shiny surface (Diamond Foil, Reynolds Metals Co., 555 Guthridge Court, Norcross, GA 30092) was treated with an aqueous solution of monoclonal antibody specific for *E. coli* 0157 (Product C65310M, Biodesign International, 60 Industrial Park Road, Saco, Maine 04072 USA) at an approximate concentration of 18 microgram per milliliter. The solution was at near pH 5.0, so as to increase the number of protonated carboxylic acid moieties on the protein for interaction with the aluminum oxide surface. The solution was kept in contact with the aluminum foil for approximately 20 minutes and then the aluminum foil was rinsed with deionized water. The aluminum was next rinsed with a concentrated solution of sodium chloride and sucrose and then allowed to air dry. In this example, the aluminum foil was used for the base member (120), the monoclonal antibodies formed the binding agent layer (140), and sodium chloride and sucrose made up the packaging layer (150). In this example, the natural aluminum oxide serves as chemical entity (132). While the antibodies were applied to the shiny side of the aluminum foil, an organic semiconductor was applied to the matte side, specifically opposite the location of the bound binding agent layer. Phthalate-containing commercial nail polish (Product No. 53 from A. Atar, Israel) was used as the semiconductive element (198). Another suitable nail polish is Orly® Nail Color, Orly International, 9309 Deering Avenue, Chatsworth, CA 91311-5856, USA). It is believed that a dibutylphthalate component in the nail polish acts as an organic semiconductor capable of receiving electrons from the aluminum base member and receiving holes from gold of the second conductive element (197). The polish was allowed to dry and strips were cut with approximate dimensions of 1 cm x 4 cm. Individual strips were placed partially in an Eppendorf tube with the nail polish-treated side of the aluminum foil exposed for contact with electrodes attached to a Fluke 189 multimeter, having data collection software, which was used for the detection unit (170). Gold coated black and red banana leads of

the Fluke 189 multimeter were used as the electrode (161) and the electrode (160) respectively. The black banana lead was contacted to the nail polish-treated surface, while the red banana lead was contacted directly to the aluminum foil. A gold coating on the black banana lead served as the second conductive element (197).

Reference is now made to Fig. 2, which is a signal time plots of the output of the Fluke 189 multimeter taken during exposure of a sensor strip, prepared according to this example, to the turkey-water suspension as a background experiment. As shown in a plot (200), there was no significant signal produced. When gold coating of the black banana lead contacted the semiconductor, at a point (202), rectified signal current produced a negative signal. The lowest reading recorded over an interval of six minutes was –0.06 microamperes, as indicated by a point (204). This sample was shown by plating and standard bacteriological culture to contain non-target bacteria, and not to contain the target bacterium, *E. coli* 0157:H7.

Reference is now made to Fig. 3, which is a signal time plot of the output of the Fluke 189 multimeter. A plot (300) was taken during exposure of another sensor strip, prepared according to this example, to the same turkey-water suspension, after the suspension had been spiked with *E. coli* 0157:H7 that had been stored frozen and then thawed. As seen on the plot (300), a much stronger signal was recorded within one minute, as compared with the plot (200) (Fig. 2). Over the course of the experiment, signals exceeding 25 microamperes were recorded, for example at a point (302) and at a point (304). Quantitative bacteriological culture by routine plating of the stock material used for the experiment indicates that the number of colony-forming units (cfu's) in the one milliliter sample tested was approximately 30,000.

Removal of the gold from the black banana lead, electrode (161), resulted in loss of signal, while removal of gold coating from the red banana lead, electrode (160), which was directly in contact with the aluminum foil used as the base member (120), did not cause any change in sensor performance.

It was found that covering the gold plating of the electrode (161) that serves as the second conductive element (197) with aluminum when the electrode is in contact with the nail polish consistently resulted in cessation of signal during active experiments. It is be-

lieved that the work function of aluminum is inappropriate for delivery of holes to the component of the nail polish that functions as the semiconductive element (198) . Additionally, nitrocellulose present in the nail polish appears to prevent direct contact between the second conductive element (197), namely the gold coating on the electrode (161) with aluminum foil of the base member (120).

Second embodiment.

Reference is now made to Fig. 4, which is a schematic of a sensor detection system (400) that is constructed and operative in accordance with an alternate embodiment of the invention. The sensor detection system (400) is similar to the sensor detection system (100) (Fig. 1), and like elements have like reference numerals, advanced by 300. In the sensor detection system (400), the chemical entity (132), the packaging layer (150), and the second conductive element (197) are omitted. A second conductive element (497) is integral with a sensor strip (422), having an area of contact with a semiconductive element (498) at a position (467). An electrode (461) is moved into a contacting relationship at a position (499) with the second conductive element (497) during operation, as indicated by the double-pointed arrow in Fig. 4.

Example 2.

Using the embodiment of Fig. 4, a conducting polymer is employed as a base member (420). On one side, antibodies for blood-related virus antigens are immobilized to form a binding agent layer (440). The layer is briefly treated with dilute glutaraldehyde to effect partial cross-linking and lattice stabilization. On the opposite side of the base member, a polymeric semiconductor coating is applied to the second conductive element (497) to form the semiconductive element (498). The sensor strip (422) is contacted to two electrodes (460, 461) of a digital voltmeter-based detection unit, which is used as a detection unit (470). One of the electrodes (460, 461) is contacted directly to the base member at position (465), while the other one of the electrodes (460, 461) is contacted to the semiconductive element (498) at the position (467). A drop of whole blood (not shown) is placed on the sensor strip (422), on the same side as the binding agent layer (440). If a viral antigen is present in the drop of whole blood (not shown), then its

interaction with the binding agent layer (440) will lead to a reading or indication in the detection unit (470).

Third Embodiment.

Reference is now made to Fig. 5, which is a schematic of a sensor detection system (500) that is constructed and operative in accordance with an alternate embodiment of the invention. The sensor detection system (500) is similar to the sensor detection system (100) (Fig. 1), and like elements have like reference numerals, advanced by 400. A second conductive element (597) is integral with a sensor strip (522), having an area of contact with a semiconductive element (598) at a position (567). An electrode (561) is in a contacting relationship at a position (599) with the second conductive element (597). The semiconductive element (598) contacts a base member (520) of the sensor strip (522) directly.

Example 3.

In this example, a metal foil serves as the base member (520). A non-conducting chemical entity (532) is applied to one side of the foil. On the same side of the foil as the chemical entity (532), a binding agent layer (540) is formed above the chemical entity (532) by soaking the coated foil in a solution of single-strand nucleic acid binding agents. A packaging layer (550) is formed above the binding agent layer (540) by soaking the sensor strip (522) in a solution of sodium chloride and sucrose. A detection unit (570) is a digital ammeter, with a first electrode (560), and a second electrode (561), the electrode (561) being coated with a deposited layer to form the second conductive element (597) of indium tin oxide at its electrode tip. Above the indium tin oxide is deposited an organic polymer, which serves as the semiconductive element (598). The electrode (560) is contacted to the sensor strip (522), directly at the base member at position (565). The second electrode (561) with associated indium tin oxide and semiconductive element is similarly contacted to the sensor strip (522) at a position (567). A drop of blood (not shown) is applied to the packaging layer (550), which dissolves to expose the binding agent layer (540). If the analyte DNA single strand is present in the blood, then a current will be generated in a closed sensor circuit (520, 560, 570, 561, 597, 598). In this exam-

ple, the electrode (561) is coated with a metal having a high work function, indium tin oxide, which serves as the second conductive element (597), while the organic polymer deposited over the indium tin oxide serves as the semiconductive element (598)

Fourth Embodiment.

Reference is now made to Fig. 6, which is a schematic of a sensor detection system (600) that is constructed and operative in accordance with an alternate embodiment of the invention. The sensor detection system (600) employs multiplexed sensor strips for multiple analyte detection. A plastic substrate (601), for example polyethylene, is coated with conducting ink lines (621, 622). On each of the conductive ink lines (621, 622) is bound a binding agent layer (641, 642) of a unique antibody specific for a given food pathogenic bacteria, thereby defining two sensing units (625, 635). Each of the ink lines (621, 622) is contacted by two unique leads (661, 662, 663, 664) of a detection unit (670). Two separate semiconductive elements (698, 699) are externally located in the detection unit (670), each of the semiconductive elements (698, 699) forming a component of a first sensor circuit (670, 698, 662, 625, 661), and a second sensor circuit (670, 699, 664, 635, 663). The operation of the sensing units (625, 635) is similar to the operation of the sensor strip (122) of the sensor detection system (100) (Fig. 1), although the physical arrangement and structure are different.

Example 4.

A liquefied food sample is applied to the sensing units (625, 635). The presence of a given pathogenic bacterium causes a generated electrical signal to be recorded in one of the first sensor circuit (670, 698, 662, 625, 661), or the second sensor circuit (670, 699, 664, 635, 663), whichever circuit is associated with the antibody binding agent specific for the given bacterial agent present in the sample.

Fifth Embodiment.

Reference is now made to Fig. 7, which is a schematic of a sensor detection system (700) that is constructed and operative in accordance with an alternate embodiment of the invention. A glass substrate (701) is coated with an opaque layer of indium tin ox-

ide that forms a second conductive element (723). The second conductive element (723) is partially coated with a polymer to form a semiconductive element (798). A base member (720) is formed by a coating of aluminum metal that is applied on top of the semiconductive element (798), and the segment (727) of the second conducting element (723) that is not masked by the semiconductive element (798). A binding agent layer (740) is immobilized above the base member (720). A sample with analyte (757) is applied to the binding agent layer (740). The presence of the analyte (757) causes electrons from the aluminum of base member (720) and holes from the indium tin oxide of the second conductive element (723) to combine in the semiconductive element (798) and form excitons. Breakdown of the excitons leads to the emission of photons (729), which indicates presence of the analyte (757). The photons (729) are suitably amplified and processed by appropriate signal processing circuitry (not shown), and both the presence and the quantitation of the photons (729) may be recorded using conventional automatic data processing techniques.

The work function of the indium tin oxide of the second conductive element (723) is higher than that of the semiconductive element (798), and is appropriate for hole donation into the semiconductive element (798). Hole donation occurs even in the absence of a physically connected detection unit. The sensor detection system (700) can operate without a physically connected detection unit or associated electrodes. It is possible to detect the presence of the analyte (757) by a remote detecting unit (770), such as a photosensitive device or material, having suitable optics and spatial resolution, so that the remote detecting unit (770) can monitor many instances of the sensor detection system (700) simultaneously. In some embodiments, it is possible for the user to detect emission of the photons (729) using direct vision, in which case the remote detecting unit (770) can be entirely omitted.

In some embodiments the semiconductive element (798) can be a multilayered OLED. The presence of additional electron transport and hole transport layers (not shown) or other coatings may greatly enhance signal generation efficiency during analyte detection or quantification.

Sixth embodiment.

Reference is now made to Fig. 8, which is a schematic of a sensor detection system (800) that is constructed and operative in accordance with an alternate embodiment of the invention. The sensor detection system (800) is similar to the sensor detection system (100) (Fig. 1), and like elements have like reference numerals, advanced by 700. A sensor strip (822) is exposed to a sample (853) that contains target analyte (855). Typically, the sample (853) is disposed in a fluid container (856). A detection unit (870) is coupled to the sensor strip (822) and to a semiconductive element (898) via a pathway (871). In some embodiments the pathway (871) can be realized as an electrode, in which case a second electrode (873), indicated as a broken line in Fig. 8, connects the detection unit (870) to a base member (820).

In other embodiments the pathway (871) can be an optical pathway, in which case the electrode (873) is omitted, and the sensor strip (822) is constructed similar to the sensor strip (722) (Fig. 7). The sample (853) and the sensor strip (822) may be remote from the detection unit (870), and there need not be direct physical contact with the detection unit (870). Remote detection capability is an important feature of the sensor detection system (800). The implications of remote detection are that nearly any material that can be recognized at a level of specificity by a peptide, protein, antibody, enzyme, receptor, nucleic acid single strand, synthetic binding agent, or the like can be detected and quantified safely in food, body fluids, air or other samples quickly, cheaply, and with high sensitivity. Remote detection also enhances the utility of the sensor detection system (800) in hazardous environments, or in locations where the presence of an operator is impractical.

Response is very rapid, generally less than 90 seconds. Cost of manufacture is low, and sensitivity has been shown to be sufficiently high for practical analyte detection.

The present invention has been described with a certain degree of particularity, however those versed in the art will readily appreciate that various modifications and alterations may be carried out without departing from the spirit and scope of the following claims. Therefore, the embodiments and examples described here are in no means intended to limit the scope or spirit of the methodology and associated devices related to the present invention.

Claims.

1. A sensor for detecting an analyte, comprising:

a base member having a conductive property, said base member defining a first conductive element;

a binding agent layer proximate said base member;

a semiconductive element proximate said base member; and,

a second conductive element that is electrically contacted to said semiconductive element and said first conductive element; wherein said base member and said binding agent layer define a sensor strip.

2. The sensor according to claim 1, further comprising a chemical entity bound to said base member and disposed between said base member and said binding agent layer.

3. The sensor according to any of claims 1 - 2, further comprising two equipotential leads coupling said sensor strip to a detection unit, wherein at least one of said equipotential leads is electrically contacted to said semiconductive element.

4. The sensor according to claim 1, wherein a work function of said second conductive element is less than a work function of said semiconductive element and said work function of said second conductive element is greater than a work function of said base member.

5. The sensor according to any of claims 1 – 4, wherein said second conductive element is an element of an electrode connected to a detection unit, said second conductive element being brought into contact with said semiconductive element, wherein said semiconductive element is an element of said sensor strip.

6. The sensor according to any of claims 1 – 5, further comprising a packaging layer disposed above said binding agent layer, said packaging layer being soluble in a medium that contains the analyte..

7. The sensor according to any of claims 1 – 5, wherein said semiconductive element is an organic compound and is physically associated with said base member on a first side of said base member, wherein said binding agent layer is immobilized on a second side of said base member.

8. The sensor according to any of claims 1 – 5, wherein said sensor strip comprises a plurality of sensor strips.

9. The sensor according to any of claims 1 – 5, wherein said semiconductive element is electroluminescent.

10. A method for detecting a predetermined analyte, comprising the steps of:

providing an electrically conductive base member, said base member defining a first conductive element;

forming a binding agent layer of macromolecules in proximity to said base member, wherein said macromolecules are capable of interacting at a level of specificity with said predetermined analyte,

disposing a semiconductive element proximate said base member, wherein said base member, said binding agent layer and said semiconductive element define a sensor strip;

exposing said predetermined analyte to said binding agent layer; and,

detecting an electrical current generated in a closed electrical circuit, said electrical current being responsive to a presence of said predetermined analyte, wherein said closed electrical circuit comprises said base member, said semiconductive element, and a second conductive element electrically contacted to said semiconductive element.

11. The method according to claim 10, further comprising the steps of:
binding a chemical entity to said base member; and
forming said binding agent layer proximate said chemical entity.

12. The method according to any of claims 10 – 11, wherein said step of detecting is performed by equipotentially coupling leads of a detection unit to said sensor strip, wherein one of said leads is coupled to said semiconductive element.

13. The method according to claim 12, wherein said step of coupling said detection unit is performed by contacting electrodes to said sensor strip and said semiconductive element, electrical passivity of said electrodes being maintained while performing said step of coupling.

14. The method according to claim 13, wherein said second conductive element is physically associated with one of said electrodes prior to performing said step of coupling.

15. The method according to any of claims 10 - 11, wherein a work function of said conductive element is less than a work function of said semiconductive element and said work function of said conductive element is greater than a work function of said base member.

16. The method according to any of claims 10 - 11, wherein said semiconductive element is an organic compound and is physically associated with said base member on a first side of said base member, wherein said binding agent layer is immobilized on a second side of said base member.

17. The method according to any of claims 10 – 11, further comprising the step of disposing a packaging layer above said binding agent layer, said packaging layer being soluble in a medium that contains said predetermined analyte.

18. The method according to any of claims 10 – 11, further comprising the step of generating photonic energy in said closed electrical circuit.

19. The method according to claim 18, wherein said step of detecting comprises detecting said photonic energy.

20. The method according to claim 19, wherein said photonic energy is detected remote from said sensor strip.

21. The method according to claim 10, wherein said sensor strip comprises a plurality of sensor strips.

22. A sensor for the detection of an analyte through generated electroluminescence, comprising:

an electrically conductive base member, said base member defining a first conductive element;

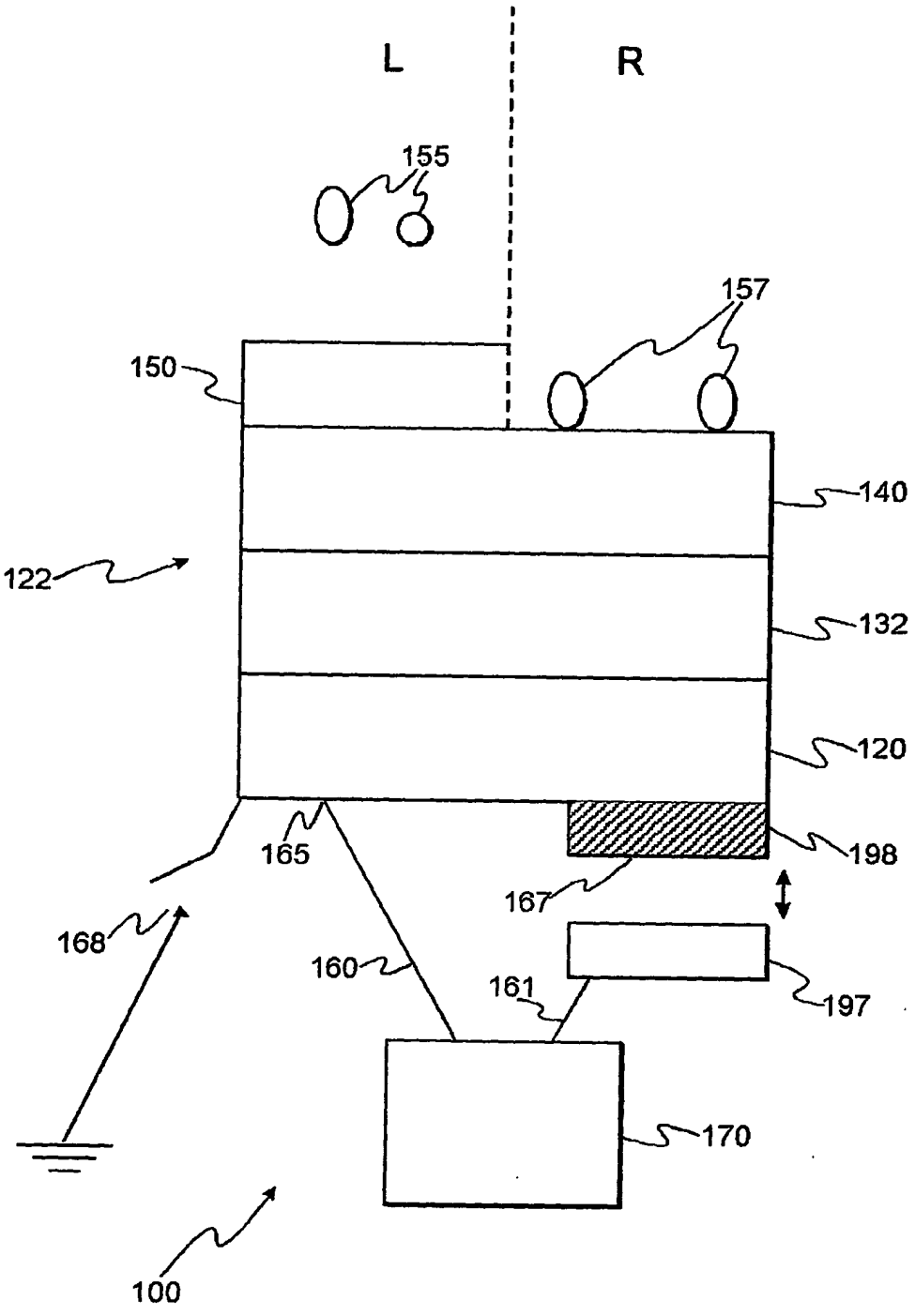
a binding agent layer proximate said base member;

an electroluminescent semiconductive element proximate said base member; and

a second conductive element that is electrically contacted to said base member and said semiconductive element.

23. The sensor according to claim 22, wherein a work function of said second conductive element is less than a work function of said semiconductive element and said work function of said second conductive element is greater than a work function of said base member.

24. The sensor according to claim 22, wherein said second conductive element is optically opaque.


L
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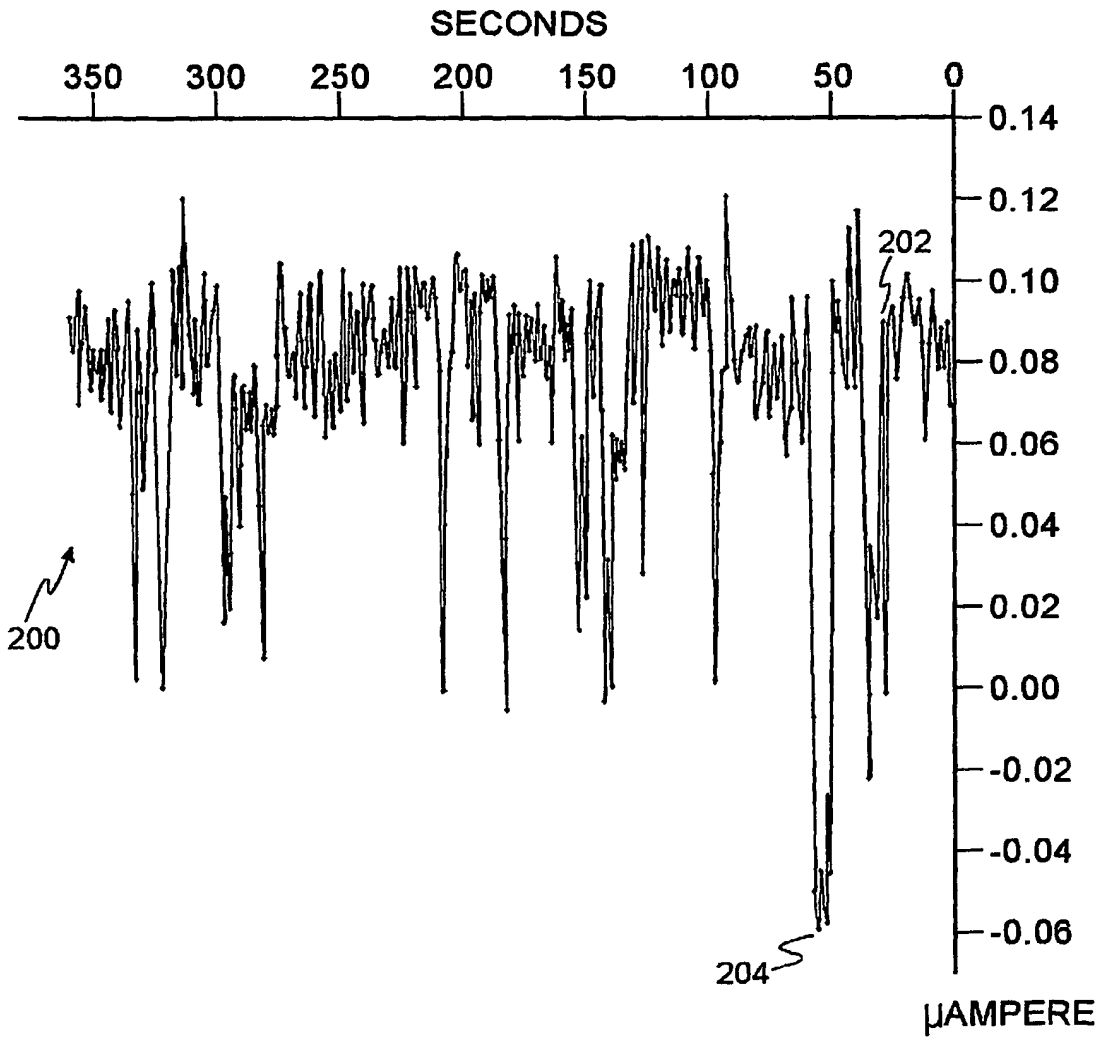
170
100

FIG. 1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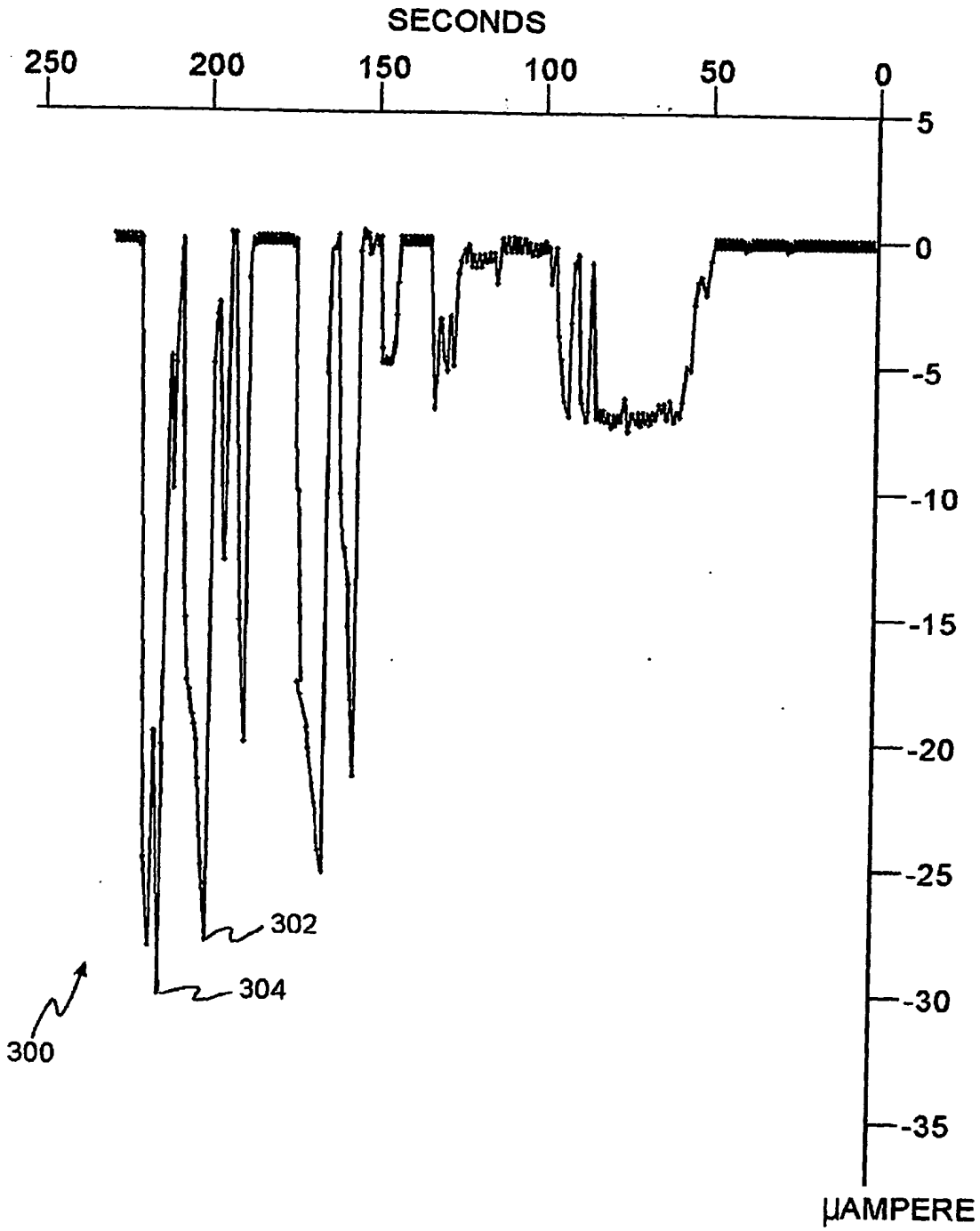
μAMPERE

FIG. 2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300

FIG. 3

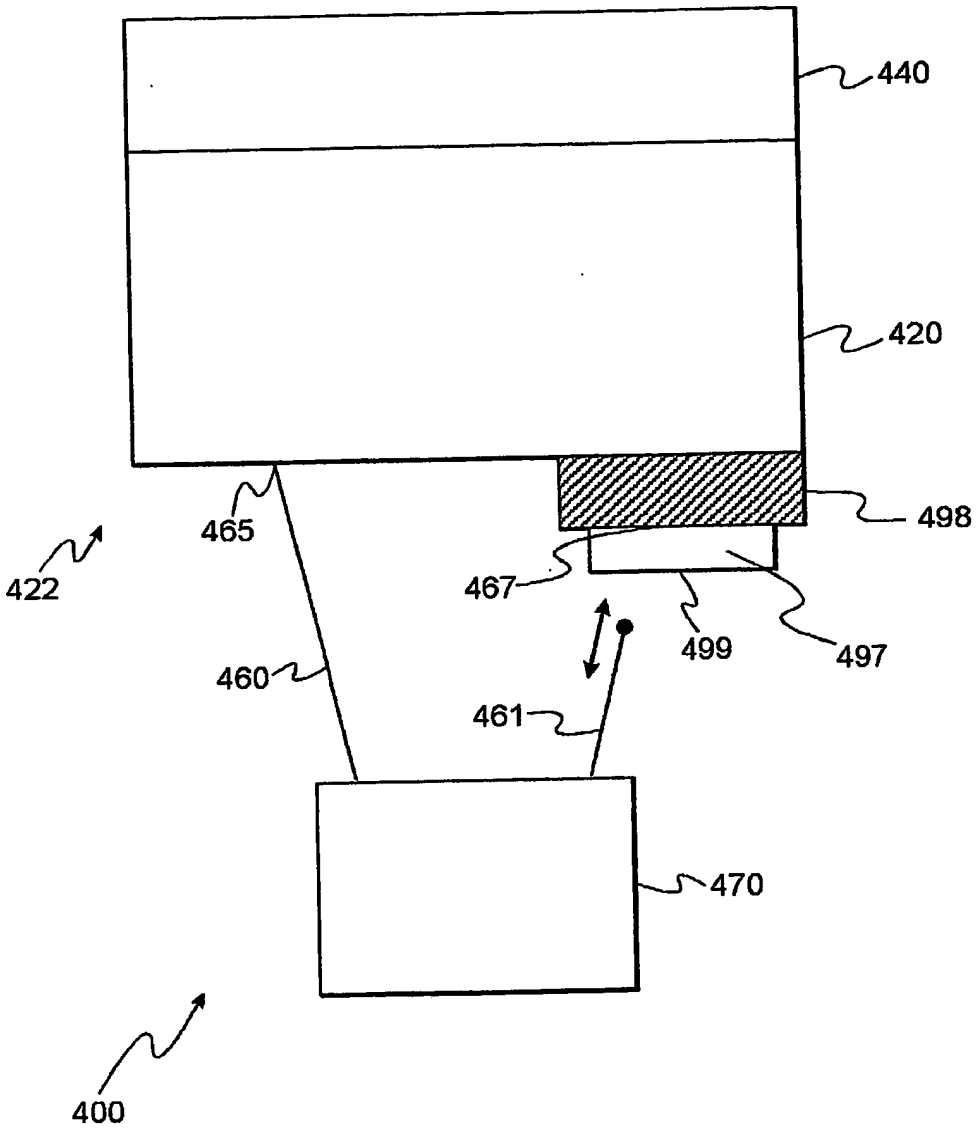

FIG. 4

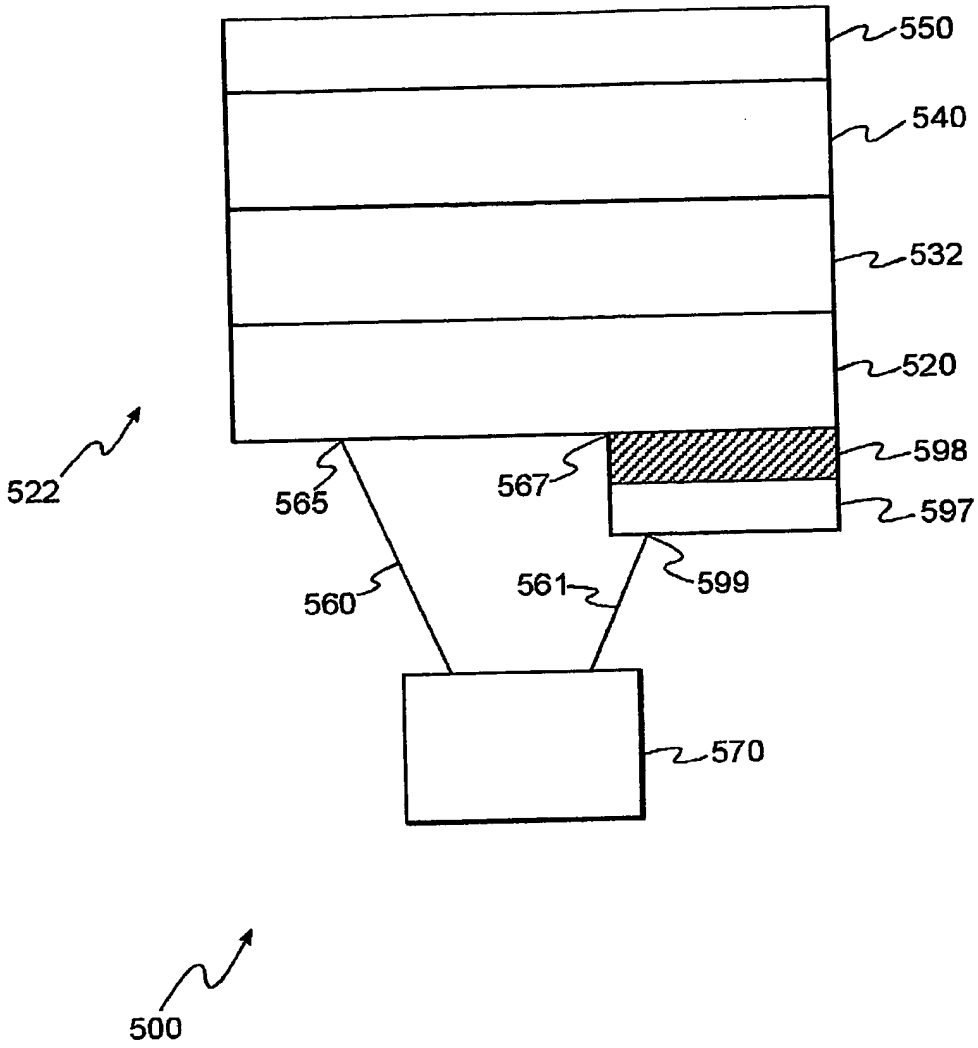

FIG. 5

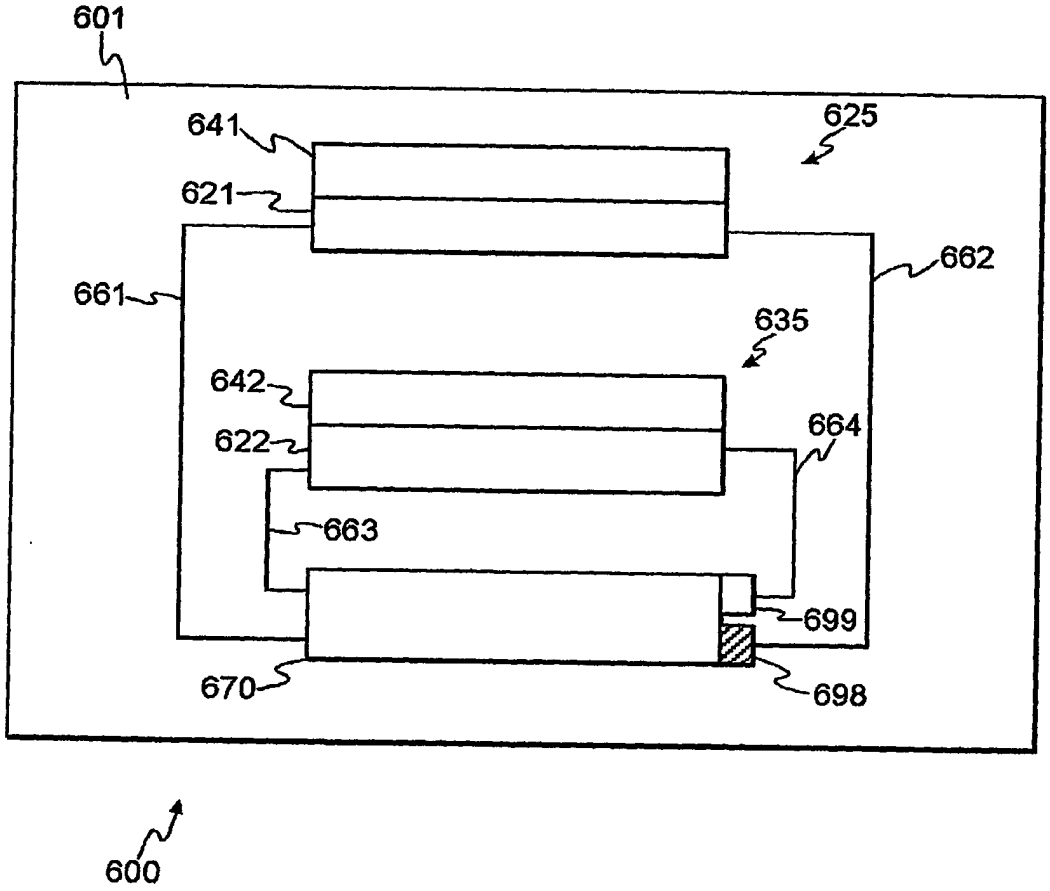

FIG. 6

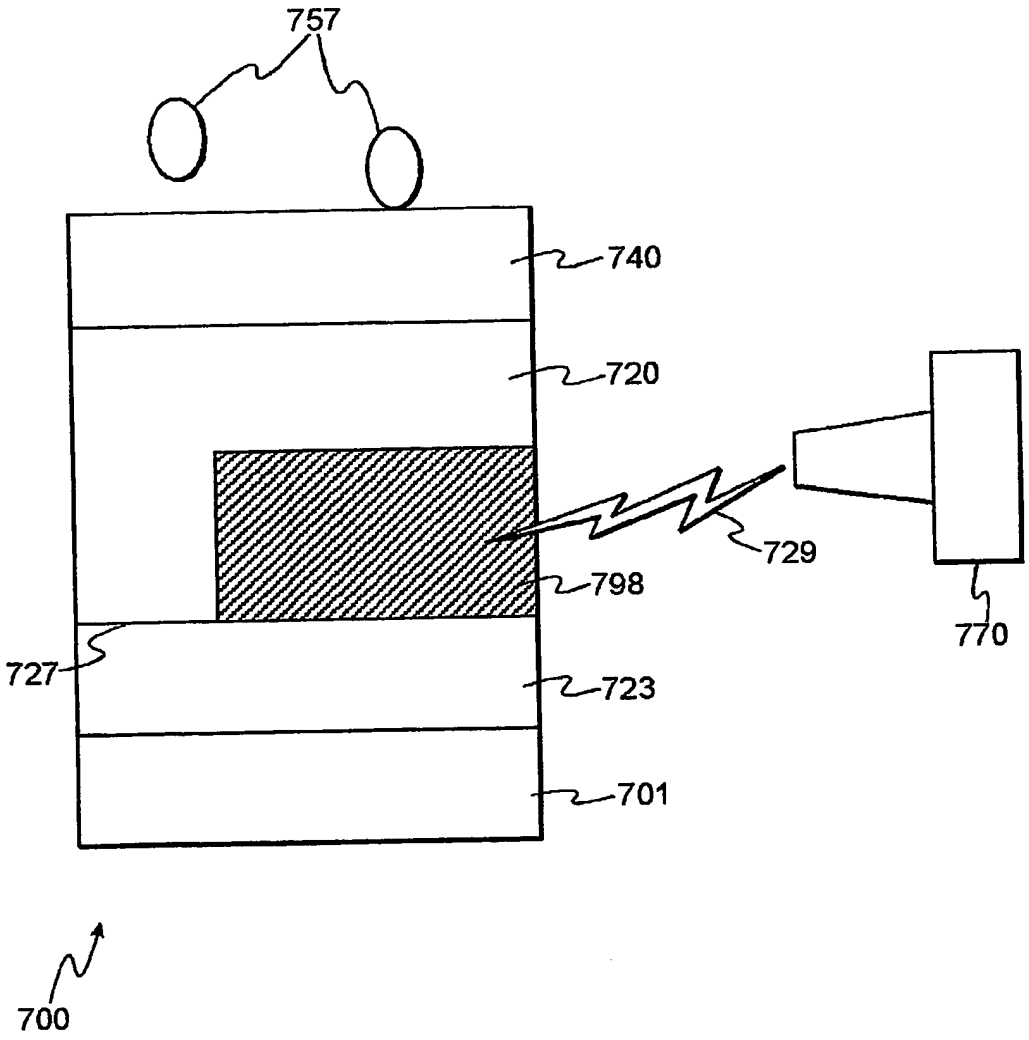

FIG. 7

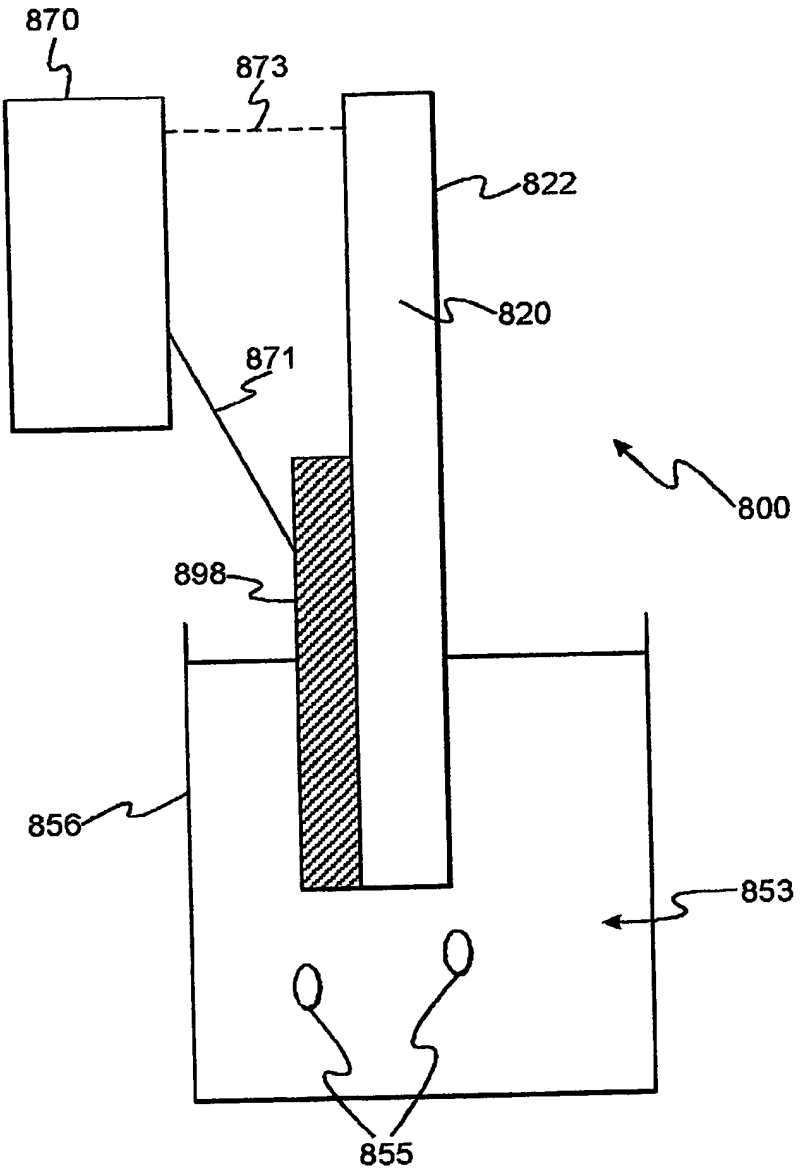

FIG. 8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/29791

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :G01N 33/543, 33/487

US CL :422/82.01, 82.02, 82.05, 82.08; 436/524, 525, 527, 151, 172

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 422/82.01, 82.02, 82.05, 82.08; 436/524, 525, 527, 151, 172

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,096,497 A (BAUER) 01 August 2000, entire document.	1-24
X	WO 99/66322 A1 (BIOSENSOR SYSTEMS DESIGN, INC.) 23 December 1999, entire document.	1-24
A	US 4,839,017 A (TANIGUCHI et al) 13 June 1989, entire document.	1-24
A	US 5.482,855 A (YAMAFUJI et al) 09 January 1996, entire document.	1-24
A	EP 0,441,120 A (YEDA RESEARCH AND DEVELOPMENT CO., LTD.) 14 August 1991, entire document.	1-24

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
11 DECEMBER 2001	02 JAN 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JEFFREY R. SNAY Telephone No. (703) 308-0661

Form PCT/ISA/210 (second sheet) (July 1998)*